

REMARKS

Claims 1-19 are pending in the application. Claim 1 has been amended to recite an apparatus with a "sample port" and a "reagent port." Support for the amendment can be found at page 8, paragraph 26, of the application. New claims 20-25 have been added. Support for the new claims can be found throughout the specification, particularly at page 9, paragraph 29 through page 10, paragraph 30 and figures 3A-3C and figure 4. No new matter has been added.

Amendment of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and was done solely to more particularly point out and distinctly claim the invention to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Rejection of Claims 1-19 under 35 U.S.C. 112

Claims 1-19 have been rejected under 35 U.S.C. 112 as being indefinite.

In particular, the Office Action states that with regard to claim 1, it is not clear from the instant claim language whether or not various elements are intended to be part of the positively claimed apparatus.

In response, Applicant has amended claim 1 to positively recite certain claim elements and to more clearly define the claimed invention. As amended, claim 1 is directed to a flow-through cell block embedding apparatus with a cell flow pathway defined by an inflow tube adapted to be coupled to a sample port for delivering cell fragments from a cell sample to the sample port. The sample port is in fluid communication with a tissue cassette having attached thereto a filter, the cell flow pathway being configured so that, upon the application of pressure from a pressure source, the cell fragments are drawn from the cell sample through the inflow tube to the sample port and deposited onto the filter. In addition, the apparatus also has a reagent flow pathway defined by a plurality of reagent delivery tubes adapted to be coupled to a reagent port for delivering a plurality of reagents to the reagent port in communication with the sample port, the reagent flow pathway being configured so that, upon the application of pressure from a pressure source, the reagents are drawn through the reagent delivery tubes to the reagent port and to the deposited cell fragments on the filter.

Thus, the claimed apparatus requires two flow pathways, a cell flow pathway and a reagent flow pathway. The apparatus, also requires two ports, the sample port and the reagent port, which are both in communication with each other. In light of these amendment, the claim is more clearly defined, and Applicant respectfully requests, the Examiner to withdraw the rejection.

With regard to claim 2, which speaks to an apparatus that “further comprising a tissue cassette in fluid communication with the sample port and the reagent port such that the cell fragments are automatically deposited near the plane to be sectioned by a microtome.” The Office Action asserts that the “further limitation of claim 2 appears to be related to the tissue cassette and filter which have not been positively recited.”

In response, Applicant respectfully traverses the rejection. Applicant has amended claim 2 to positively recite a tissue cassette in fluid communication with the sample port and the reagent port, thereby rendering the rejection moot with regard to this claim. The tissue cassette apparatus is important for the operation of the apparatus to capture cells from the cell sample, to allow preparation of the cells for tissue sectioning, and to retain the cells in a plane desirable for tissue sectioning without further manipulation. In fact, Applicant teaches that the tissue cassette and filter allows the cells to be deposited in a plane at which the microtome blade will cut the cell block without further manipulation (*See* page 11, lines 2-6). This avoids manual handling of the sample and reduces the risk of cross contamination. The tissue cassette and filter may be provided separately. Thus, the further limitation of claim 2 is not indefinite with regard to the tissue cassette and filter.

With regard to claim 3-6, which recite the application of “pressure,” the Office Action asserts that “claim 1 and claims 3-6 fail to positively recite a source for applying pressure.”

Claims 3-6 depend from claim 1, which has now been amended to positively recite a pressure source, thereby rendering the rejection moot with regard to these claims.

With regard to claims 11-14 and 18, the Office Action asserts that since “claim 1 does not positively recite the filter, cassette and/or sample port as part of the claimed device, it is not clear what further structure is defined in view of the positively recited elements of claim 1.”

In response, Applicant respectfully traverses the rejection. Claims 11-14 and 18 depend from amended claim 1. Amended claims 11-12 are directed to a “filter that is removably and replaceably positioned adjacent to the tissue cassette.” Claims 13-14 are directed to “a cylindrical port” that can be attached to the filter and the sample port. Claim 18 is directed to a “disposable” sample port.

Again, Applicant emphasizes that the filter and tissue cassette are removable and replaceable components of the apparatus. The filter may be removed from the tissue cassette, and can be made of a number of different materials, such as polycarbonate. In addition, the tissue cassette may have a cylindrical port that allows attachment to a gasket and filter, and to the sample port. As these components are required for the operation of the apparatus and are functionally described in claim 1, it is Applicant’s position that claims 11-14 are adequately defined. Claim 18 depends from claim 1, which has been amended to recite a “sample port,” thereby rendering the rejection moot.

For all the foregoing reasons, Applicant respectfully requests the Examiner to withdraw the rejection.

Rejection of Claims under 35 U.S.C. 103

Claims 1-7, 9-14, 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shiina *et al.* (JP 2000-146782) in view of Aeikens *et al.* (DE 2928790).

The Office Action asserts that with respect to claim 1, Shiina *et al.* “discloses a cell embedding device that includes a *reagent flow pathway* defined by a plurality of reagent delivery tubes (*See Fig. 1, elements 6-8*)...in communication with a sample/reagent port (2) in communication with a filter (1).” However, as the Office Action concedes, this reference *does not disclose* the “use of a cell flow pathway or inflow tube for delivering cells from a cell sample to a port in communication with the filter.”

The Office Action also asserts that Aeikens *et al.* discloses that “it is known in the art to provide cells to a cell collection filter for tissue processing using a cell flow pathway (1) that includes a cell sample and an inflow tube for delivering the cells to a sample port

(3).” Based on these two references, the Examiner concludes that it would have been obvious to one of ordinary skill in the art to provide the “cell sample required of the primary reference using the system of the reference of Aeikens *et al.* for the known and expected result of providing an art recognized means for providing a cell sample to a filter for cell/tissue processing techniques.”

Applicant respectfully traverses this rejection. To establish a *prima facie* case of obviousness “there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references) must teach or suggest all the claim limitations.” See M.P.E.P. 2143. Furthermore, “[b]oth the suggestion and the expectation of success must be founded in the prior art, not in Applicant’s disclosure” *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.* 927 F.2d 1200, 1207, 18 USPQ2d 1016 (Fed. Cir. 1991) quoting *In re Dow Chemical Corp.*, 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988).

For reasons discussed in detail below, the Shiina *et al.* and Aeikens *et al.* references cited by the Examiner lack the necessary suggestion and motivation to combine their teachings to arrive at the claimed invention.

The claimed invention is directed to an apparatus with two flow pathways, the cell flow pathway and the reagent flow pathway. In addition, the apparatus requires two separate ports, the reagent port and the sample port, where the reagent port is in communication with the sample port. The fluids from each respective flow path and port pass into the tissue cassette and filter which captures the cell fragments and allows the cells to be embedded in an orientation that is conducive for microtome processing.

Shiina *et al.* discloses an apparatus that produces cell samples for microscopic investigation. In contrast to the claimed invention, Shiina *et al.* has a plurality of reagent tubes that are in contact with one “sample/reagent port.” There is no teaching or suggestion in Shiina *et al.* for two separate ports associated with two separate flow pathways where the reagent port is in communication with the sample port. In fact, in Shiina *et al.*, the samples are injected into the sample port by an operator, and then the

reagents are administered into the same sample port. Based on the teaching in Shiina *et al.*, the skilled artisan would not be motivated to use separate flow paths or an apparatus with two separate ports.

This deficiency is not made up for by Aeikens *et al.*, who merely teaches how to load cells onto a filter attached to a syringe. The cells are fixed onto the filter, and the filter converted from an opaque state to a transparent state for observation through a microscope. In contrast to the claimed invention, Aeikens *et al.* only describe one flow pathway in which cells from a syringe are delivered onto a filter, that Examiner labels as a “sample port.” Aeikens *et al.* do not teach or suggest an apparatus that has two flow pathways, with two separate ports, and where the reagent port is in communication with the sample port.

Based on the teachings of Shiina *et al.* and Aeikens *et al.*, the skilled artisan, at most would have used one flow pathway and one port. There is no motivation available in either reference to combine their teaching to arrive at the claimed invention. Accordingly, each reference, either alone, or in combination fails to render the claimed invention obvious.

Claims 2-6, have been rejected as being obvious in light of Shiina *et al.* and Aikens *et al.* because “the combination of the references discussed above is considered to meet the instant claim language.”

Applicant respectfully traverses the rejection. Claim 2 is directed to an apparatus in which “a tissue cassette [is] in fluid communication with the sample port and the reagent port such that the cell fragments are automatically deposited near the plane to be sectioned by a microtome.” Claims 3-6 are directed to the application of “pressure” to the reagent flow pathway and the cell flow pathway. Claims 2-6 depend from amended claim 1, which requires two flow pathways and two ports. The arguments presented above for Shiina *et al.* and Aikens *et al.* are reiterated here in their entirety. For all the reasons discussed above, Shiina *et al.*, and Aikens *et al.* fail to render the claimed invention obvious.

Claim 7 has been rejected because “the tubes disclosed by the reference of Shiina *et al.* is [sic] capable of delivering any of the listed reagents.”

Applicant respectfully traverses the rejection. Claim 7 depends from amended claim 1, which requires an apparatus with two flow pathways and two ports, the reagent port and the sample port. The arguments presented above for Shiina *et al.* and Aikens *et al.* are reiterated here in their entirety.

Claims 9 and 10 have been rejected because “the reference of Shiina *et al.* discloses the use of pumps ...and valves ... for controlling the flow of reagent to the filter.”

Applicant respectfully traverses the rejection. Claims 9 and 10 depend from amended claim 1, which requires two flow pathways and two ports. The arguments presented above for Shiina *et al.* and Aikens *et al.* are reiterated here in their entirety.

Claims 11-14 have been rejected because according to the Office Action, “the filter and tissue cassette have not been positively recited as part of the claimed device and the system of the modified primary reference would be capable of being provided in communication with a tissue cassette housing a removable filter.”

Applicant respectfully traverses the rejection. As stated above, the tissue cassette and filter are components that are required for the apparatus, but may be provided separately from the apparatus. Thus, it is Applicant’s position that claims 11-14, directed to a filter or a cylindrical port associated with the tissue cassette, are adequately defined by claim 1.

With regard to claims 18 and 19, Applicant requests clarification of the rejection because it is not apparent from the Office Action what the Examiner considers to be the basis of the rejection. However, in order to be responsive, Applicant respectfully traverses the rejection. As claims 18 and 19 depend upon amended claim 1, the arguments presented above are reiterated here in their entirety.

In light of the amendments to claim 1 and the arguments presented, Applicant respectfully requests that the Examiner withdraw the rejection.

Rejection of Claim 8 under 35 U.S.C. 103

Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Shiina *et al.* (JP 2000-146782) in view of Aeikens *et al.* (DE 2928790) taken further in view of Weiskopf (US 3,227,130). In particular, the Office Action asserts that claim 8 is rejected because “Weiskopf discloses that it is known in the art of tissue processing to include a tube heater...”

Applicant respectfully traverses the rejection. Claim 8 depends from amended claim 1. The arguments presented for Shiina *et al.* and Aeikens *et al.* under the section entitled “Rejection of claims under 35 U.S.C. 103,” are reiterated here in their entirety. The Shiina *et al.* and Aeikens *et al.* either alone, or in combination fail to teach an apparatus with two flow pathways and two ports. This deficiency not is remedied by Weiskopf, who merely describes how to prepare tissue for microscopic examination and includes a heating wire to heat liquid. Weiskopf therefore fails to teach or suggest an apparatus with two flow pathways and two ports.

Accordingly, the Examiner is respectfully requested to withdraw the rejection.

Rejection of Claims 1-7, 9-11, and 13-19 under 35 U.S.C. 103

Claims 1-7, 9-11 and 13-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shiina *et al.* (JP 2000-146782) in view of Aeikens *et al.* (DE 2928790) taken further in view of Williamson, *et al.* (DS 5,817,032). The Office Action fails to give any particular reason for the rejection.

However, in order to be responsive, Applicant respectfully traverses the rejection. The rejected claims are not obvious in view of the combination of Shiina *et al.* and Aeikens *et al.* for all the reasons discussed above under the section entitled “Rejection of claims under 35 U.S.C. 103.” Williamson, *et al.* fails to remedy the discrepancy because this reference only describes a filter for trapping tissue, replacing the tissue fluid with wax, and then slicing the supporting material and tissue using a microtome. There is no teaching or suggestion for two flow pathways, for two ports and that the reagent port is in communication with the sample port.

Claims 15-17 are rejected under 35 U.S.C. 103(a) as being obvious in view of Shiina *et al.* and Williamson, *et al.* Claims 15-17 are directed to a “waste container.” The Office Action asserts that although “Shiina *et al.* does not disclose a waste container, Williamson, *et al.* discloses that it is known in the art to employ a waste container.”

Applicant respectfully traverses the rejection. Claims 15-17 depend from amended claim 1. As stated above Shiina *et al.* fails to disclose an apparatus with two flow pathways and two ports where the reagent port is in communication with the sample port. This deficiency is not remedied by Williamson *et al.* who simply describes a filter system. Williamson, *et al.* fails to teach or suggest an apparatus with two flow pathways and two ports.

Accordingly, the Examiner is respectfully requested to withdraw the rejection.

Rejection of Claim 8 under 35 U.S.C. 103

Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Shiina *et al.* (JP 2000-146782) in view of Aeikens *et al.* (DE 2928790) and Williamson, *et al.* taken further in view of Weiskopf (US 3,227,130) because claim 8 includes “a heated tube,” and Weiskopf discloses that “it is known in the art to use a tube heater.”

Applicant respectfully traverses the rejection. Claim 8 depends from amended claim 1, which requires an apparatus with two flow pathways and two ports. The arguments presented under the section entitled “Rejection of claims 1-7, 9-11 and 13-19 under 103,” are reiterated here in their entirety. Thus, Shiina *et al.* Aeikens *et al.* and Williamson, *et al.* either alone, or in combination, fail to teach or suggest the claimed invention. This discrepancy is not remedied in Weiskopf, who describes how to prepare tissue for microscopic examination and includes a heating wire to heat liquid, but fails to teach or suggest an apparatus with two flow pathways and two ports.

Accordingly, the Examiner is respectfully requested to withdraw the rejection.

Rejection of Claim 12 under 35 U.S.C. 103

Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Shiina *et al.* (JP 2000-146782) in view of Aeikens *et al.* (DE 2928790) and Williamson, *et al.* taken further in view of Liu *et al.* (US 5,691,633).

The Office Action asserts that Shiina *et al.*, Aeikens *et al.* (DE 2928790) and Williamson, *et al.* “fail to disclose the use of a polycarbonate filter,” but that “Liu *et al.* discloses that the use of polycarbonate as a cell filter is well known in the art.”

Applicant respectfully traverses the rejection. Claim 12 depends from amended claim 1 which requires an apparatus with two flow pathways and two ports. For all of the reasons provided above under the section entitled “Rejection of claims 1-7, 9-11 and 13-19 under 103” these references alone, or in combination, fail to teach or suggest an apparatus with two flow pathways and two ports. This discrepancy is not remedied by Liu *et al.* who describes an apparatus for determining the electrical property of a cell sample. The specific section of Liu *et al.* used in the Office Action to support the rejection, simply describes how to determine the impedance characteristic of cells embedded in a polycarbonate filter. There is no teaching or suggestion in Lui *et al.* for an apparatus with two flow pathways and two ports.

For all the forgoing reasons, the references, either alone, or in combination, fail to render the claimed invention obvious. Accordingly, the Examiner is respectfully requested to withdraw the rejection.

New Claims

New claims 20-25 have been added and are directed to a tissue cassette assembly for cell block embedding. The tissue cassette assembly has a cassette body with a port that extends from the top surface to a bottom surface of the tissue cassette body. The region of the port extending from the top surface is adapted to be in fluid communication with a sample or a reagent, and the region of the port extending from the bottom surface is adapted to be in communication with a removable gasket, which provides a fluid tight seal. The tissue cassette assembly also has a filter that is in contact with the removable gasket. The filter is positioned to be in a plane desired for tissue sectioning using a tissue sectioning device such as a microtome.

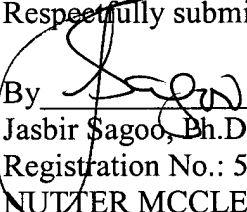
This filter captures the cell fragments from a cell sample and allows the captured fragments to be prepared for tissue sectioning using washing and embedding reagents. As a result, the captured cells are prepared for sectioning without the need of manual manipulation of the sample, thus reducing the risk of cross contamination of the sample.

Conclusion

In view of the foregoing remarks, reconsideration of the rejections and allowance of all pending claims is respectfully requested. If a telephone conversation with Applicant's representative would expedite prosecution of the above-identified application, the Examiner is urged to call Applicant's representative at (617) 439-2994.

Dated: September 17, 2004

Respectfully submitted,

By 
Jasbir Sagoo, Ph.D.
Registration No.: 51,177
NUTTER MCCLENNEN & FISH LLP
World Trade Center West
155 Seaport Boulevard
Boston, Massachusetts 02210-2604
(617) 439-2000
(617) 310-9000 (Fax)
Applicant's Representative